Frudakis and Shriver

Application No.: 10/644,594

Filed: August 19, 2003

Page 2

PATENT Attorney Docket No.: DNA1170-2

## Amendments to the Claims

Please amend claims 1, 24, 31, 39-42, 45, 48, 50-51, 53-54 and 56-57 as indicated in the listing of claims.

Please cancel claims 2, 7, 10-11, 13-14, 17-20, 23, 25-28, 33-36, 38, 46 and 59-82 without prejudice or disclaimer.

The listing of claims will replace all prior versions, and listings of claims in the application:

## **Listing of Claims:**

- 1. (Currently Amended) A method of inferring, with a predetermined level of confidence, a trait of an individual, comprising:
  - a) contacting a sample comprising nucleic acid molecules of a test individual with hybridizing oligonucleotides,

wherein the hybridizing nucleotides can detecting, in a nucleic acid sample from an individual, nucleotide occurrences of single nucleotide polymorphisms (SNPs) of in a panel of at least about ten ancestry informative markers (AIMs), wherein the nucleotide occurrences of the SNPs are indicative of a population structure, wherein the population structure is correlated with the a trait of the individual, and wherein the panel comprises at least one AIM that is not linked to a gene linked to the trait, and

wherein said contacting is performed under conditions suitable for detecting the nucleotide occurrences of the AIMs of the test individual by the hybridizing oligonucleotides; and

b) identifying with a predetermined level of confidence, a the population structure that correlates indicated by with the nucleotide occurrences of the SNPs AIMs detected in

Frudakis and Shriver

Application No.: 10/644,594

Filed: August 19, 2003

Page 3

the test individual of step a), wherein identifying the population structure correlates withinfers a the trait,

**PATENT** 

Attorney Docket No.: DNA1170-2

thereby inferring, with a predetermined level of confidence, the trait of the individual.

- 2. (Cancelled)
- 3. (Original) The method of claim 1, wherein the trait comprises biogeographical ancestry (BGA).
- 4. (Original) The method of claim 3, wherein the panel comprises AIMs set forth as SEQ ID NOS:1 to 331.
- 5. (Original) The method of claim 3, wherein the panel comprises AIMs set forth as SEQ ID NOS:1 to 71.
  - (Original) The method of claim 3, wherein the panel comprises AIMs set forth as:
    SEQ ID NOS:7, 21, 23, 27, 45, 54, 59, 63, and 72 to 152;
    SEQ ID NOS:3, 8, 9, 11, 12, 33, 40, 59, 63, and 153 to 239;
    SEQ ID NOS:1, 8, 11, 21, 24, 40, 172, and 240 to 331; or
    combinations thereof.
  - 7. (Cancelled)

Frudakis and Shriver

Application No.: 10/644,594

Filed: August 19, 2003

Page 4

- 8. (Original) The method of claim 3, wherein the BGA comprises a proportion of a sub-Saharan African, Native American, IndoEuropean, or East Asian ancestral group, or a combination of said ancestral groups.
- 9. (Original) The method of claim 8, wherein the BGA comprises a proportion of at least three ancestral groups.

**PATENT** 

Attorney Docket No.: DNA1170-2

10 and 11. (Cancelled)

12. (Original) The method of claim 1, wherein the trait comprises responsiveness of the individual to a drug.

13 and 14. (Cancelled)

- 15. (Original) The method of claim 1, wherein the trait comprises susceptibility to a disease.
  - 16. (Original) The method of claim 15, wherein the disease has an ethnic predisposition.

17 to 20. (Cancelled)

- 21. (Original) The method of claim 15, wherein the disease is alcoholism.
- 22. (Original) The method of claim 1, wherein the trait comprises a pigmentation trait.
- 23. (Cancelled)

Frudakis and Shriver

Application No.: 10/644,594

Filed: August 19, 2003

Page 5

24. (Currently Amended) The method of claim 1, further comprising identifying, with a predetermined level of confidence, a sub-population structure of the population structure indicated by that correlates with the nucleotide occurrences of the AIMs-SNPs detected in the test individual in step a), wherein the sub-population structure correlates infers with a the trait.

**PATENT** 

Attorney Docket No.: DNA1170-2

25 to 28. (Cancelled)

- 29. (Original) The method of claim 1, which is performed in a high throughput format.
- 30. (Original) The method of claim 1, which is performed in a multiplex format.
- 31. (Currently Amended) A method of estimating, with a predetermined level of eonfidence, proportional ancestry of at least two ancestral groups of an individual, comprising:
  - a) contacting-detecting, in a nucleic acid sample from a sample comprising nucleic acid molecules of an test individual, with hybridizing oligonucleotides,

wherein the hybridizing oligonucleotides can detect nucleotide occurrences of single nucleotide polymorphisms (SNPs) of in a panel of at least about ten ancestry informative markers (AIMs), wherein the nucleotide occurrences of the SNPs are indicative of a population structure, wherein the population structure is correlated with biogeographical ancestry (BGA) for each of the at least two ancestral groups, and wherein the panel comprises at least one AIM that is not linked to a gene linked to BGA examined, and

wherein said contacting is under conditions suitable for detecting the nucleotide occurrences of the AIMs of the test individual by the hybridizing oligonucleotides; and

Frudakis and Shriver

Application No.: 10/644,594

Filed: August 19, 2003

Page 6

b) identifying, with a predetermined level of confidence, a the population structure that correlates indicated by with the nucleotide occurrences of the AIMs SNPs of each of the ancestral groups examined detected in the individual of step a), wherein identifying the population structure is indicative estimates of proportional ancestry,

**PATENT** 

Attorney Docket No.: DNA1170-2

thereby estimating, with a predetermined level of confidence, proportional ancestry of the individual.

32. (Original) The method of claim 31, wherein the proportional ancestry comprises a proportion of a sub-Saharan African ancestral group, a Native American ancestral group, an IndoEuropean ancestral group, an East Asian ancestral group, or a combination thereof.

33 to 36. (Cancelled)

37. (Original) The method of claim 31, wherein the panel for at least one of the ancestral groups comprises AIMs set forth as:

SEQ ID NOS:7, 21, 23, 27, 45, 54, 59, 63, and 72 to 152; SEQ ID NOS:3, 8, 9, 11, 12, 33, 40, 59, 63, and 153 to 239; SEQ ID NOS:1, 8, 11, 21, 24, 40, 172, and 240 to 331; or combinations thereof.

- 38. (Cancelled)
- 39. (Currently Amended) The method of claim 31, wherein the-proportional ancestry comprises proportions of three ancestral groups, and

wherein identifying a-the population structure that correlates withindicated by the nucleotide occurrences of the AIMs-SNPs of the test-individual of step a) comprises:

Frudakis and Shriver

Application No.: 10/644,594

Filed: August 19, 2003

Page 7

PATENT Attorney Docket No.: DNA1170-2

performing a likelihood determination for affiliation with each of a sub-Saharan African ancestral group, a Native American ancestral group, an IndoEuropean ancestral group, and an East Asian ancestral group;

thereafter selecting three ancestral groups having a greatest likelihood value;

determining a likelihood of all possible proportional affiliations among the three ancestral groups having the greatest likelihood value, whereby a population structure or proportional affiliation-that correlates with the nucleotide occurrences of the AIMs-SNPs of the test-individual is identified; and

identifying a single proportional combination of maximum likelihood, thereby estimating the proportional ancestry of the individual.

40. (Currently Amended) The method of claim 31, wherein the proportional ancestry comprises proportions of three ancestral groups, and wherein identifying a population structure that correlates withindicated by the nucleotide occurrences of the AIMs-SNPs comprises:

performing six two-way comparisons comprising likelihood determinations for affiliation between each group with each other group;

thereafter selecting three ancestral groups having a greatest likelihood value;

determining a likelihood of all possible proportional affiliations among the three ancestral groups having the greatest likelihood value, whereby a population structure or proportional affiliation that correlates with the nucleotide occurrences of the AIMs-SNPs of the test-individual is identified; and

identifying a single proportional combination of maximum likelihood, thereby estimating the proportional ancestry of the individual.

41. (Currently Amended) The method of claim 31, wherein the proportional ancestry comprises proportions of three ancestral groups, and

Frudakis and Shriver

Application No.: 10/644,594

Filed: August 19, 2003

Page 8

wherein identifying a-the population structure that correlates with indicated by the nucleotide occurrences of the AIMs-SNPs of the test-individual of step a) comprises:

**PATENT** 

Attorney Docket No.: DNA1170-2

performing three three-way comparisons among the groups,

determining a likelihood of all possible proportional affiliations among the three ancestral groups having the greatest likelihood value, whereby a population structure or proportional affiliation that correlates with the nucleotide occurrences of the AIMs-SNPs of the test-individual is identified; and

identifying a single proportional combination of maximum likelihood, thereby estimating the proportional ancestry of the individual.

42. (Currently Amended) The method of claim 31, wherein the proportional ancestry comprises proportions of four ancestral groups, and

wherein identifying a-the population structure that correlates withindicated by the nucleotide occurrences of the AIMs-SNPs of the test-individual of step a) comprises performing six two-way comparisons, three three-way comparisons, or one four-way comparison among the four ancestral groups;

determining a likelihood of all possible proportional affiliations among the four ancestral groups having the greatest likelihood value, whereby a population structure or proportional affiliation-that correlates with the nucleotide occurrences of the AIMs-SNPs of the test-individual is identified; and

identifying a single proportional combination of maximum likelihood, thereby estimating the proportional ancestry of the individual.

43. (Original) The method of claim 40, further comprising generating a graphical representation of the comparison of the three ancestral groups, said graphical representation comprising a triangle with each an-ancestral group independently represented by a vertex of the

Frudakis and Shriver

Application No.: 10/644,594

Filed: August 19, 2003

Page 9

triangle, wherein the maximum likelihood value of proportional affiliation for an individual comprises a point within the triangle.

**PATENT** 

Attorney Docket No.: DNA1170-2

- 44. (Original) The method of claim 43, wherein the graphical representation further comprises a confidence contour indicating a level of confidence associated with estimating the proportional ancestry.
- 45. (Currently Amended) The method of claim 31, further comprising identifying, with a predetermined level of confidence, a sub-population structure of the population structure that eorrelates indicated by with the nucleotide occurrences of the AIMs in the test individual, wherein the sub-population structure correlates infers with ethnicity of the test individual.
  - 46. (Cancelled)
- 47. (Original) The method of claim 45, wherein the ancestral group is IndoEuropean, and wherein the ethnicity comprises Northern European or Mediterranean.
- 48. (Currently Amended) The method of claim 31, further comprising generating an ancestral map of the world, wherein locations of populations having a proportional ancestry corresponding to the proportional ancestry of the test-individual are indicated on the ancestral map.

Frudakis and Shriver

Application No.: 10/644,594

Filed: August 19, 2003

Page 10

49. (Original) The method of claim 48, further comprising

a) overlaying the ancestral map with a genealogical map, wherein the genealogical map indicates locations of populations having geopolitical relevance with respect to the test individual, and

PATENT

Attorney Docket No.: DNA1170-2

- b) statistically combining the information of the ancestral map and genealogical map to obtain a most likely estimate of family history of the test individual.
- 50. (Currently Amended) The method of claim 31, wherein identifying a population structure that correlates with indicated by the nucleotide occurrences of the AIMs SNPs detected in the individual of step a) comprises comparing the nucleotide occurrences of the AIMs SNPs of the test-individual with known proportional ancestries corresponding to nucleotide occurrences of AIMs SNPs indicative of BGA.
- 51. (Currently Amended) The method of claim 50, wherein the known proportional ancestries corresponding to nucleotide occurrences of AIMs SNPs indicative of BGA are contained in a database.
- 52. (Original) The method of claim 51, wherein the comparing is performed using a computer.
- 53. (Currently Amended) The method of claim 50, wherein each of the known proportional ancestries corresponding to nucleotide occurrences of AIMs-SNPs indicative of BGA further comprises of at least one photograph of a person from whom the known proportional ancestry was determined.

Frudakis and Shriver

Application No.: 10/644,594

Filed: August 19, 2003

Page 11

54. (Currently Amended) The method of claim 53, wherein the <u>at least one</u> photograph comprises a digital photograph.

PATENT

Attorney Docket No.: DNA1170-2

- 55. (Original) The method of claim 54, wherein digital information comprising the digital photograph is contained in a database.
- 56. (Currently Amended) The method of claim 55, wherein the digital information in the database is associated with a-the known proportional ancestry corresponding to nucleotide occurrences of AIMs-SNPs indicative of BGA of the person in the photograph.
- 57. (Currently Amended) The method of claim 51, further comprising identifying at least one photograph of a person having a proportional ancestry corresponding to the proportional ancestry of the test-individual.
- 58. (Original) The method of claim 57, wherein identifying the photograph comprises scanning a database comprising a plurality of files, each file comprising digital information corresponding to a digital photograph of a person having a known proportional ancestry, and identifying at least one photograph of a person having nucleotide occurrences of AIMs indicative of BGA that correspond to the nucleotide occurrences of AIMs indicative of BGA of the test individual.

59-82 (Cancelled)